

identical to said target gene in said animal cell, and wherein the two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence, wherein the other of said two structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence, and wherein the two structural sequences are spaced from each other by a nucleic acid
stuffer fragment.

48. A genetic construct according to any one of claims 2, 3, 34-36 or 46 wherein at least one of the structural gene sequences is 20 or 30 nucleotides long.

49. A method according to any one of claims 40-43, 45 or 47 wherein at least one of the structural gene sequences is 20 or 30 nucleotides long.

REMARKS

Claims 1, 4, 37, 39 and 44 have been canceled without prejudice.

The remaining claims have been amended to substitute the term "synthetic gene" with the term "genetic construct". Although the term "synthetic gene" is defined in the specification at page 7, lines 1-3, Applicant has amended the claims to use the term "genetic construct" in an effort to expedite prosecution.

The claims have been further amended to substitute the term "multiple" with the recitation "at least two". Support for this amendment is found in the specification, e.g., at page 16, lines 20-22.

Added claim 46 is directed to one preferred genetic construct of the present invention, which comprises two structural gene sequences in opposite orientations. Added claim 47 is

directed to one preferred method of delaying or repressing the expression of a target gene by expressing a genetic construct which comprises two structural gene sequences in opposite orientations. Support for claims 46-47 is found in the specification, e.g., at page 16, lines 20-22.

Added claims 48-49 are directed to a genetic construct of a particular length and a method of using such genetic construct. Support for these claims is found in the specification, e.g., at page 10, lines 23-24.

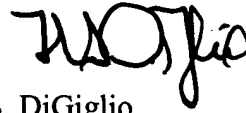
It is respectfully submitted that the instant amendments to the claims do not introduce new matter.

Furthermore, Applicants submit herewith a Declaration by Dr. Graham under 37 C.F.R. §1.132 (**Exhibit 1**, with annexures labeled as MWG 1 to 11), in further support of the enablement of the constructs and methods presently claimed. More specifically, the declaration presents data which demonstrate the successful use of various genetic constructs, as presently claimed, in suppressing the expression of a target gene in an animal cell. The articles referenced at page 12, line 8-10 of the Declaration are also enclosed as **Exhibits 2-3**.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment. The attached is captioned "**Version with markings to show changes made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Frank S. DiGiglio
Registration No. 31,346

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, New York 11530
Telephone: 516-742-4343

FSD/XZ:ab
Encls.: Version with Markings to Show Changes Made
Exhibits 1-3

Serial No: 09/100,812
Docket: 11535

Version With Markings To Show Changes Made

IN THE CLAIMS:

Please cancel claims 1, 4, 37, 39 and 44 without prejudice.

Please amend claims 2, 3, 34-36, 38-42 and 45 as follows:

2. (Twice Amended) A [synthetic gene] genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell, which is transfected with said [synthetic gene] genetic construct in the cell, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural gene sequences, wherein each of said structural gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region or derivative of said target gene, and wherein said [multiple] at least two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence.

3. (Twice Amended) A [synthetic gene] genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell, which is transfected with said [synthetic gene] genetic construct in the cell, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural gene sequences wherein each of said structural gene sequences is separately placed under the control of a promoter which is operable in said cell, and wherein each of said structural gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region

or derivative of said target gene, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of an individual promoter sequence.

34. (Amended) A [synthetic gene] genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said [synthetic gene] genetic construct in the cell, wherein said synthetic gene comprises [multiple] at least two structural gene sequences, wherein each of said structural gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region or derivative of said target gene, and wherein said [multiple] at least two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence and wherein at least one other of said structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence.

35. (Amended) A [synthetic gene] genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said [synthetic gene] genetic construct in the cell, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural gene sequences and each of said structural gene sequences is separately placed under the control of a promoter which is operable in said cell, and wherein each of said structural gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region or derivative of said target gene, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other of said

structural gene sequences is placed operably in the antisense orientation under the control of another individual promoter sequence.

36. (Amended) A [synthetic gene] genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said [synthetic gene] genetic construct in the cell, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural gene sequences, wherein each of said structural gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region or derivative of said target gene, and wherein said [multiple] at least two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence, wherein at least one other of said structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence, and wherein said at least one structural gene sequence that is placed in the sense orientation relative to said promoter and said at least one structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

38. (Amended) A cell comprising the [synthetic gene] genetic construct of any one of claims [1] 2-3, 34-36 or [35-37] 46.

40. (Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising transfecting said animal cell with a [synthetic gene] genetic construct, wherein said [synthetic gene] genetic construct comprises a structural gene sequence comprising a nucleotide sequence which is substantially identical to the nucleotide sequence of said target gene, or a region or derivative of said target gene, wherein said structural gene is placed operably

in the sense orientation under the control of a promoter which is operable in said cell, thereby delaying or repressing the expression of said target gene in said animal cell.

41. (Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising transfecting said animal cell with a [synthetic gene] genetic construct, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural [genes] gene sequences, wherein each of said structural [genes] gene sequences comprises a nucleotide sequence which is substantially identical to the nucleotide sequence of said target gene, or a region or derivative of said target gene, and wherein said [multiple] at least two structural [genes] gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one of said structural [genes] gene sequences is placed operably in the sense orientation under the control of said promoter sequence.

42. (Amended) The method according to claim 41, wherein at least one other of said structural [genes] gene sequences is placed operably in the antisense orientation under the control of said promoter sequence.

45. (Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising [transfecting] expressing in said animal cell [with a synthetic gene] a genetic construct, wherein said [synthetic gene] genetic construct comprises [multiple] at least two structural [genes] gene sequences, wherein each of said structural gene sequences is separately placed under the control of a promoter which is operable in said cell, and wherein each of said structural [genes] gene sequences comprises a nucleotide sequence which is substantially identical to said target gene, or a region or derivative of said target gene, wherein at

least one of said structural gene sequences is placed operably in the sense orientation under the control of an individual promoter sequence.

Please add claims 46-49:

46. A genetic construct comprising two structural gene sequences, wherein each of said structural gene sequences is identical to a target gene in an animal cell, and wherein the two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence, wherein the other of said two structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence, and wherein the two structural sequences are spaced from each other by a nucleic acid stuffer fragment.

47. A method of delaying or repressing the expression of a target gene in an animal cell, comprising expressing in said animal cell a genetic construct, wherein said genetic construct comprises two structural gene sequences, wherein each of said structural gene sequences is identical to said target gene in said animal cell, and wherein the two structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence, wherein the other of said two structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence, and wherein the two structural sequences are spaced from each other by a nucleic acid stuffer fragment.

48. A genetic construct according to any one of claims 2, 3, 34-36 or 46 wherein at least one of the structural gene sequences is 20 or 30 nucleotides long.

49. A method according to any one of claims 40-43, 45 or 47 wherein at least one of the structural gene sequences is 20 or 30 nucleotides long.